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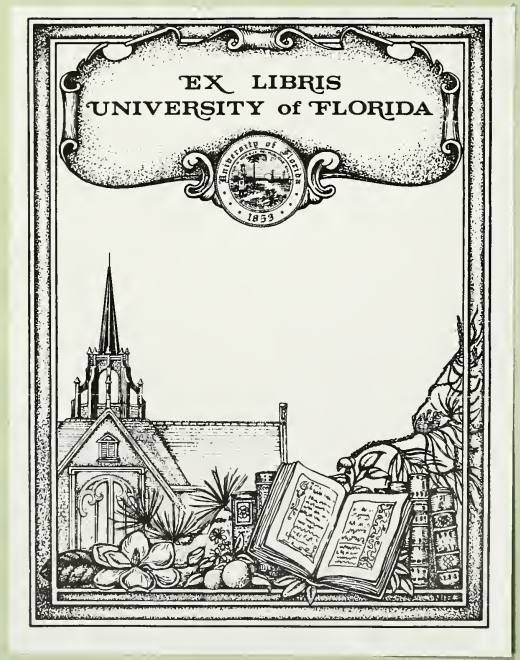
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MANKIND'S GREAT NEED
POPULATION RESEARCH

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The Population Crisis Committee is an incorporated non-profit educational organization which seeks to stimulate public awareness, understanding and action in the face of the greatest population increase mankind has ever experienced.

MANKIND'S GREAT NEED
POPULATION RESEARCH

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PREFACE

President Nixon, in concluding his historic message to Congress on population, said, "One of the most serious challenges to human destiny in the last third of this century will be the growth of the population. Whether man's response to that challenge will be a cause for pride or for despair in the year 2000 will depend very much on what we do today." In that message in enumerating government action which should be undertaken without delay, he stated, "First, increasing research is essential."

Secretary-General of the United Nations U Thant, in addressing a meeting in New York on February 24, 1971, said, "The greatest contribution that the developed countries can make . . . for all the peoples of the world is in the field of research and development . . . to develop safer and more effective methods of fertility control."

Pope Paul VI in his Encyclical Letter, *Humanae Vitae,* includes a strong plea to men of science "who can considerably advance the welfare of marriage and the family, along with peace of conscience, if by pooling their efforts they labor to explain more thoroughly the various conditions favoring a proper regulation of births."

Despite the consensus of world leaders, despite the strong reinforcement of their opinions by responsible individuals in all phases of population activity, the results of research in human fertility and reproduction are slow in reaching the mothers and fathers of families and are insufficient to meet their needs.

In an effort to assess what could and should be done in this situation, Lawrence R. Kegan, Executive Director of the Population Crisis Committee, approached leading scientists working in the field of population. Each is a recognized authority in his own specialty. These scientists were asked to give us a short nontechnical statement of what could and should be done in his own field and, to the best of his ability, to give us his estimate of a reasonable level of funding required to produce useful results.

We were assisted in our task of selecting the authorities and in fitting their statements within the confines of this pamphlet by outstanding generalists in the field of population research. We also consulted the Science Advisors to our recent Presidents and Nobel prize winners in the fields of physiology and medicine. Their reactions are recorded here.

The funding estimates of the scientists whom we questioned total from $250 million a year in 1971 to almost $400 million in 1975. These totals are the sums of uncoordinated estimates which were not subject to budget constraints. Nevertheless, one cannot read the words of the scientists, portraying existing deficiencies and the possibilities for advancement, without concluding that there is an imperative need and a great opportunity to help mankind here and now.

One must further conclude that the responsible committees of the U.S. Senate and the House of Representatives were taking considered, prudent, and wise action when they drew up the Family Planning Services and Population Research Act of 1971. Their prudence and wisdom, both from the standpoint of budgetary constraints and in terms of the needs of their countrymen, are evident in their authorizations for population research. They authorized increased funding, over and above the $28 million appropriated in 1971, in the amount of $30 million for 1971, $50 million for 1972, and $65 million in 1973.

Andrew P. O'Meara
National Chairman
Population Crisis Committee

July, 1971

On July 28, 1971, Representative Flood, Chairman of the Subcommittee on Appropriations for the Departments of Labor and of Health, Education and Welfare and Related Agencies, in his Report on the bill for 1972 stated:

> *"Population research is primarily concerned with the development of new contraceptives, the evaluation of current contraceptives and the behavioral aspects of population growth, distribution and restraint. As all existing methods of birth control are unsatisfactory, in one way or another, there is a still unmet need for a contraceptive method or device that will be reliably effective, safe for use over a long period of time, simple enough to be self-administered, inexpensive, and socially, esthetically and psychologically acceptable to a wide spectrum of population groups. It must also be possible to cease the use or reverse the effect of the method so that normal conception may take place without residual danger to mother or child. At present it appears unlikely that one method can meet all these criteria. The goal of contraceptive research is, therefore, to develop a number of reliable and safe contraceptive methods and devices that will be suitable for various situations and acceptable to various groups of people."*

INTRODUCTION

SHELDON J. SEGAL, PH.D.

Vice President and Director
Biomedical Division
The Population Council
New York, New York

Chairman of Subcommittee of the Population Committee of the National Academy of Sciences, 1967-1969
Member, President's Committee on Population and Family Planning, 1968
Medal *pro meritus,* on 300th Anniversary, University of Innsbruck, 1970
Honorary Lifetime Member, Indian Society for Scientific Study of Reproduction, 1970
President, International Society for Research in Reproduction

The world, unless stricken with a great catastrophe, will have to cope with much larger numbers of people. It is not unrealistic to contemplate a world population of 10 billion when today's children are mature adults. Whether the problem be food supply, health care, educational facilities, use of natural resources, pollution of the environment or general improvement of living standards, applied to a population of 10 billion—instead of today's 3.6 billion —it is close to insoluble.

Responsibile policy makers cannot leave this heritage of incalculable dilemma to the next generation. We have a choice now. Act now to give voluntary programs of fertility limitation every chance to succeed, or, by failing to act, pass on to the world leaders of the future the disastrous consequences.

The success or failure of voluntary efforts of individuals to maintain control over their fertility depends heavily on the availability of effective, acceptable and safe contraception. The methods that exist today are not sufficient. The limitations of even the most modern method—the pill—is revealed by the statistics from an excellent clinic in a superb municipal hospital in Atlanta. During a one-and-a-half-year period, over half of the women who started to use the pill abandoned the method and about 25% had pregnancies they did not want. Let us not be deluded; we do not have methods that are anywhere near perfect. The problem is not simply to get people to use the methods that now exist. This myth has restrained us from serious action too long; we must now abandon it and commit ourselves to the real need.

The prospects for developing a variety of new, improved methods of fertility control are excellent, provided that we give our scientists the support they require. Of some thirty realistic possibilities for the near and not-so-distant future, nearly a dozen innovative approaches to contraception are in use by at least small groups of volunteers; the others are at some stage of laboratory investigation. The list of potentialities include daily pills for women that would be safer than those now available; weekly or monthly pills for men or women; a small plastic implant placed under the skin of men or women, that could last for years; sophisticated devices or procedures that would make voluntary sterilization of either men or women safer, simpler and reversible; modern forms of intrauterine or intravaginal devices that women could use safely in a variety of ways, depending on their own preferences; and, orally active natural substances that could regularize menstrual cycles and improve the rhythm method.

It is well within our scientific potential to give all couples the opportunity to make every child wanted, as well as the opportunity to prevent high-risk pregnancies that unnecessarily exact a high toll in birth defects, deaths and morbidity. The overwhelming weight of scientific opinion is that the field is ready for a major assault. Sufficient funding and emphasis on the subject of human reproduction can, for the first time in man's history on earth, give control of reproduction to all people, not just the privileged few.

To achieve this objective we need to acknowledge that our understanding of the fundamental biology of reproduction is inadequate, and to remedy this deficiency. Basic research is, after all, the prior condition of all applied technology. At the same time, we should seize upon those leads that do exist and proceed with their evaluation as rapidly as possible. Here, there is a key role for government, in partnership with both the scientific community and industry. Traditionally, the transformation of a promising laboratory finding into a practical birth control method depends on a corporate decision based on such product development considerations as sales potential, exclusivity, development cost and product liability risks. Government funding can assure that all feasible methods are evaluated fully, whether or not their development represents ideal corporate policy.

As indicated by the statements that follow, a variety of scientific disciplines are needed to enlarge our understanding of human reproduction and its regulatory mechanisms. The list includes many branches of medicine, biology, chemistry and the social sciences.

America's scientists are a national resource and they will respond to the country's need, if given the mandate and the opportunity. The contribution they can make in improving the methods of fertility control may prove to be the life sciences' most significant achievement for mankind.

GENERAL BACKGROUND

"Entering the decade of the 1970's, the world will face an even greater population explosion until science and technology can bring to the world more acceptable and effective methods to control family size."

GEORGE B. KISTIAKOWSKY, PH.D.

Professor of Chemistry
Harvard University
Cambridge, Massachusetts

Science Advisor
to President Eisenhower, 1959-1961
Priestley Award, Dickinson College, 1958
Ledlie Prize, Harvard University, 1961
Parsons Award,
American Chemical Society, 1961
Foreign Member, Royal Society
Vice President,
National Academy of Sciences, 1965-1969

POPULATION RESEARCH MORE URGENT THAN EVER

In 1963, the Committee on Science and Public Policy of the National Academy of Sciences, of which I was Chairman, issued a report on *The Growth of World Population.* The report was prepared by Dr. William McElroy, as Chairman of its Panel on Population Problems, who is now the Director of the National Science Foundation.

After looking into the complex problems associated with the growth of world population, the Committee came to the conclusion that "either the birth rate of the world must come down or the death rate must go back up."

If the birth rate is to come down, "the panel concludes from its investigations that the overall task is to achieve universal acceptance of the desirability of planning and controlling family size. An essential condition for the achievement of this objective is the awareness among people throughout the world

that voluntary planning and control of family size can and will provide better opportunities for all children and greater happiness for their parents."

The report then continues: "Science and technology must provide knowledge of the nature of the reproductive processes and simple, acceptable techniques for controlling them. Societies must make available to all people techniques that do not interfere with the necessary privacy and fulfillment of marital life."

To deal with the problems raised by the rapid growth of world population, the report recommended greatly expanded population research; increased training in demography and social and bio-medical sciences concerned with population problems; additional support of research laboratories; and greater international cooperation within the United Nations' systems.

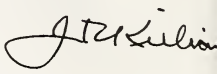
Today, eight years after that report was made, the need for large scale systematic research for better methods of voluntary fertility control and a better understanding of all the elements of population growth is still more urgently needed. Entering the decade of the 1970's, the world will face a further and even greater population explosion until science and technology can bring to all those of reproductive age throughout the world more acceptable and effective methods to control family size.

The enactment of the Family Planning Services and Population Research Act of 1970 gives strong Congressional support to the research objectives which were put forward in the 1963 report. Today, the pressures of continued world population growth make it even more urgent to expand population research to solve one of man's greatest problems.

SCIENCE ADVISORS AGREE
POPULATION RESEARCH MORE URGENT THAN EVER

The former Science Advisors to Presidents Eisenhower, Kennedy, Johnson and Nixon associate themselves with the views expressed by Dr. Kistiakowsky.

J. R. Killian, Jr.
President, Massachusetts Institute of Technology, 1948-1959
Cambridge, Massachusetts

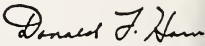


Science Advisor to President Eisenhower, 1957-1959
President's Certificate of Merit, 1948
Hoover Medal, 1963
Fellow, American Academy of Arts and Sciences

Jerome Wiesner, Ph.D.
President, Massachusetts Institute of Technology, 1971-
Cambridge, Massachusetts

Science Advisor to President Kennedy, 1961-1964
Medal of Honor, Electronic Industries Association, 1961
Fellow, American Academy of Arts and Sciences

Donald F. Hornig, Ph.D.
President, Brown University, 1971-
Providence, Rhode Island



Science Advisor to President Johnson, 1964-1969
Parsons Award, American Chemical Society, 1967
Mellon Distinguished Award, 1968
Fellow, American Academy of Arts and Sciences

Lee A. DuBridge, Ph.D.
President, California Institute of Technology, 1946-1969
Pasadena, California

Science Advisor to President Nixon, 1969-1970
Medal of Merit, 1948
Benjamin Franklin Fellow, Royal Society

NOBEL PRIZE WINNERS AGREE
POPULATION RESEARCH MORE URGENT THAN EVER

American research scientists awarded the Nobel Prize for their work in physiology and medicine associate themselves with the views expressed by Dr. Kistiakowsky.

1970

Julius Axelrod
National Institutes of Health
Bethesda, Maryland

1969

Max Delbrueck
California Institute of Technology
Pasedena, California

Alfred D. Hershey
Carnegie Institution
Cold Springs Harbor, New York

Salvador E. Luria
Massachusetts Institute of Technology
Cambridge, Massachusetts

1968

Robert W. Holley
Salk Institute
San Diego, California

Marshall W. Nirenberg
National Institutes of Health
Bethesda, Maryland

Haldan K. Hartline
The Rockefeller University
New York, New York

George Wald
Harvard University
Cambridge, Massachusetts

1966

Charles B. Huggins
University of Chicago
Chicago, Illinois

1964

Konrad Bloch
Harvard University
Cambridge, Massachusetts

1962

James Dewey Watson
Harvard University
Cambridge, Massachusetts

1961

Georg von Bekesy
University of Hawaii
Honolulu, Hawaii

1959

Arthur Kornberg
Stanford University
Stanford, California

Severo Ochoa
New York University
New York, New York

1958

Joshua Lederberg
Stanford University Medical Center
Stanford, California

Edward Laurie Tatum
Rockefeller University
New York, New York

1956

Dickinson W. Richards, Jr.
Lakeville, Connecticut

1954

John F. Enders
Medical Center
Boston, Massachusetts

Frederick Robbins
Case Western Reserve University
Cleveland, Ohio

Thomas Weller
Harvard School of Public Health
Boston, Massachusetts

1953

Fritz Lipmann
Rockefeller University
New York, New York

"There is a growing question about how long the world can survive unless it attacks, in a massive way, this complex population octopus. As a scientist who has spent 27 years on the food production front, I now urge much greater research and family planning programs on the population control front."

NORMAN E. BORLAUG, PH.D.

Director
International Maize and Wheat Improvement Center
Rockefeller Foundation
Mexico

Nobel Peace Prize, 1970

WE MUST EXPAND POPULATION RESEARCH NOW TO SLOW WORLD POPULATION GROWTH

Although I am not a scientist involved in research on reproductive biology or in family planning programs, nonetheless I feel morally obliged to express my deep concern about the lack of funding and aggressive action to support programs fighting to slow world population growth.

My professional studies and life's work have been devoted to trying to expand food production in the developing (all too often overpopulated) countries of the world. I have been one of the leaders of the so-called "Green Revolution" which in recent years has had considerable "temporary" success in increasing wheat and rice production in a number of countries. Nonetheless, the modest progress we have made can at best buy only 20 to 30 years of time on the food production front, assuming governments don't become complacent. During this brief period the world must come to grips with the frightening population monster or destroy itself.

As I stated in my speech accepting the Nobel Peace Prize: "The green revolution has won a temporary success in man's war against hunger and deprivation; it has given man a breathing space. If fully implemented, the revolution can provide sufficient food for sustenance during the next three decades. But the frightening power of human reproduction must also be curbed; otherwise, the success of the green revolution will be ephemeral only."

"Most people still fail to comprehend the magnitude and menace of the 'Population Monster'. In the beginning there were but two, Adam and Eve; when they appeared on this earth is still questionable. By the time of Christ, world population had probably reached 250 million. But between then and now population has grown to 3.5 billion. Growth has been especially fast since the advent of modern medicine. If it continues to increase at the estimated present rate of 2 percent a year, the world population will reach 6.5 billion by the year 2000. . . ."

"We must recognize the fact that adequate food is only the first requisite for life. For a decent and humane life we must also provide an opportunity for good education, remunerative employment, comfortable housing, good clothing, and effective and compassionate medical care. Unless we can do this, man may degenerate sooner from environmental diseases than from hunger."

Currently the world is not only facing a food crisis in many densely populated countries, but is ever-increasingly losing the battle on the employment and educational fronts as well. With growing unemployment there will be ever more increasing poverty, hunger and political chaos. The situation on the housing, medical care, transportation and total environmental fronts is equally grim.

There is a growing question about how long the world can survive unless it attacks, in a massive way, this complex population octopus. As a scientist who has spent 27 years on the food production front, **I now urge much greater research** and family planning programs on the population control front. Time is late and there is no time for complacency.

"There is a truly critical need for thoroughly sufficient funds to dynamize the scientific community with terrific urgency towards research into the more occult details of human reproductive physiology."

JOHN ROCK, M.D.

Clinical Professor of Gynecology, Emeritus
Harvard Medical School
Boston, Massachusetts

Co-Inventor of "the Pill"
Lasker Award,
Planned Parenthood/World Population
Ortho Award, American Gynecological Society
Fellow,
American Academy of Arts and Sciences
Honorary Member,
Societe Francaise de Gynecologie

THE SIGNIFICANCE OF POPULATION RESEARCH

Population research is the name we give to efforts to know more about all the factors of human reproduction and how best to modify one or more of them so that, harmlessly and effectively, conception may, at will, be agreeably precluded as a possible consequence of coitus. Why bother? Simply because there are already more people on earth than presently utilized resources can properly care for and because Malthus was right when he conservatively remarked, about 175 years ago, that "moral restraint is of dubious effectiveness."

While effort must be made to make available much more of Earth's untapped resources, so as to enable all people to be well fed and to live comfortably in happy communion with all, our main objective must be to restrict overall birth rates. Since the human, unlike all other species, is potentially capable of increase beyond the capacity of the environment, this is the only way humanely to hold numbers within supportive resources.

The measures Malthus listed—war, famine, and pestilence—are so unacceptable to us that instead of cultivating them to check population growth, we properly strive to check them, which makes birth control the only solution. But, given the dubious effectiveness of coital restraints there is a vital necessity to perfect methods of contraception.

Those who have any influence over allocation of actual funds, not those who merely approve budgets, must feel deeply and respond with tireless vigilance to the truly critical need for thoroughly sufficient funds to dynamize the scientific community with terrific urgency towards research into the more occult details of human reproductive physiology.

We need a coordinated team of expert scientists dedicated to ferret out the ablest researchers in the fields of physiology, immunology, enzymology, microbiology, neurobiology, electrophysiology, biochemistry, gynecology, and urology. The members of this team should scour the world for the men and women now working in these fields and prevail upon them, with irrefutable arguments and thoroughly adequate funds, to utilize to the full, institutional facilities already existing or immediately established, all firmly supported by federal and philanthropic grants.

The team should also indefatigably integrate the results of the researchers to the point of clinical usefulness. These should be widely published to the medical and sociological world and the beneficial possibilities made available to the public at large, especially to those aged 15 to 25. On their reproductive behavior depends the future of mankind.

"It is my sincere opinion that the marshalling of researchers behind the quest for voluntary and acceptable solutions to the problems of population growth is probably the single most significant contribution that can be made in this nation."

JOSEPH M. BEASLEY, M.D.

Director
Family Health, Inc.
New Orleans, Louisiana

Chairman, Executive Committee, Planned Parenthood/World Population
Member, Commission on Population Growth and the American Future
Chairman, Department of Family Health and Population Dynamics, Tulane University School of Public Health
President, Delta Omega, Honorary Public Health Society, 1970
Fellow, Royal Society of Tropical Medicine and Public Health

POPULATION RESEARCH AS SEEN BY A PROGRAM OPERATOR

At present, there is no contraceptive method that is effective, safe, inexpensive, reversible, self-administered, and acceptable to all people. What is desperately needed if our nation is to cope with the delivery of family planning services are research breakthroughs in two areas: first, a means to predict the exact moment when a woman is going to ovulate, and second, an ideal contraceptive entirely effective and free of any medical monitoring.

The basic problem with today's contraceptive technology is that it requires a high level of information and understanding; this is an overriding factor in complicating the delivery of family planning services. Some of the problems associated with today's contraceptives are:

1. They have a considerable number of side effects which call for high levels of sophistication in preparing for and dealing with failure of the

technique and consideration of a substitute method.

2. They require a relatively high educational level of the patient and family, or, in the absence of such education, inordinate communication and follow-up efforts by others.

3. They require continuous medical monitoring.

In our Louisiana program, for example, we have had to incorporate educational reinforcement as part of the physical checkup. We have had to see patients on the average of five times per year. The extreme inadequacy and inefficiency of existing contraceptive technology as we experience it in our program creates major problems in the management and logistics of the delivery service, requiring a complex system of patient services in education, communication, and management.

Thus, intricate manpower and management systems are needed to effectively deliver family planning services under the existing contraceptive technology. Actually the more sophisticated the contraceptive technology, the lower the level of education demanded for its utilization and the less complex the delivery system to implement it.

The equation is clear: the lower the sophistication of our contraceptive technology, the higher the costs of the delivery of family planning services. Conversely, the higher the level of contraceptive sophistication, the lower will be the costs. Not to mention a quantum jump in the quality of American life.

Such a breakthrough will only come through intensive and extensive research into human fertility and population dynamics. And with this nation's mounting population problems, such research cannot be conducted at a leisurely, casual pace. It must be infused with urgency and a sense of the highest priority.

It is my sincere opinion that the marshalling of researchers behind the quest for voluntary and acceptable solutions to the problems of population growth is probably the single most significant contribution that can be made in this nation.

BASIC RESEARCH IN REPRODUCTION

"Those of us who have explored basic reproductive mechanisms must confess that at this moment there is remarkably little complete information on any aspect of the reproductive processes in the human."

RICHARD J. BLANDAU, M.D.

Professor of Biological Structure
University of Washington
Seattle, Washington

BASIC RESEARCH IN REPRODUCTION: A CONFESSION OF IGNORANCE

For the past 35 years my primary research effort has been related to basic problems in reproduction such as: (1) egg and sperm development, maturation, and transport in both male and female reproductive tracts; (2) the mechanism of ovulation; (3) the mechanism of embryo orientation and attachment to the maternal endometrium; (4) the "hatching" of the embryo from the zona pellucida just before implantation; (5) the effects of aging of eggs and sperm before fertilization on their future growth and development; (6) the analysis of the proteolytic enzymes in the sperm acrosomes and their possible role in penetration of the cervical mucus and the various egg membranes at the time of fertilization; and finally, (7) the reaction of the eggs stored in the ovaries to various environmental factors such as drugs, chemicals, irradiation, etc., and the effects of these on their future growth and development.

Those of us who have explored basic reproductive mechanisms must con-

fess that at this moment there is remarkably little complete information on any aspect of the reproductive processes in the human. We do not know how spermatozoa penetrate the cervical mucus to reach the uterine lumen. We have no specific knowledge by what means spermatozoa reach the ampulla of the oviduct, the site of fertilization. No one has yet observed a normal ovulation in the human. The means by which a spermatozoon penetrates the human egg is completely unknown. The environmental requirements for the normal development of the preimplanted human egg in the oviducts and uterine cavity have not been resolved. The manner by which the embryo orients and attaches itself to invade the endometrium of the uterus is a complete mystery.

It is not an exaggeration to state that every step in the biology and physiology of reproduction in the human needs an urgent and expanded research effort so that contraceptive methods need not be based on empirical procedures. Only fundamental knowledge of reproductive processes can lead to the development of contraceptive methodology that is not empirical. Basic research in reproductive processes can and will lead to the development of a variety of methods for birth control more acceptable to various populations and with less bothersome side effects.

To accomplish this goal and to make available a number of acceptable methods for birth control will require a worldwide research effort and a recruitment of basic scientists who are not now involved in research in this field. Because of the urgency and complexity of the problem, interdisciplinary research programs must be established involving physiologists, pharmacologists, biochemists, bioengineers, immunologists, and a host of other highly skilled investigators. With adequate research support and imaginative leadership I am confident that many highly qualified researchers could be enticed into the area of basic reproductive research.

In my judgment, realistic support for research and training in the basic aspect of reproduction alone will require $100 million for 1971 and an increase to $150 million, yearly, thereafter.

"This new approach could make available a once-a-month medication, easy to administer, practically free of unwanted side effects, and at extremely small cost."

ROGER GUILLEMIN, M.D.

The Salk Institute
La Jolla, California

Louis Bonneau Prize, French Academy of Science, 1957

BRAIN HORMONES: A NEW APPROACH TO FERTILTY CONTROL

The fertility of men and women is regulated by three integrated physiological systems. The gonads (i.e. the ovaries and the testes) are controlled in their function by a small endocrine organ located at the base of the brain and called the pituitary gland. This gland is ultimately controlled by brain hormones manufactured and secreted by a small area of the brain called the hypothalamus.

The brain hormones secreted by the hypothalamus are relatively simple molecules which will be readily synthesized when their complete molecular structures are known. We propose to synthesize analogues of these molecules which will act as antagonists. Availability of these antagonists should permit us to inhibit or modify at will the functions of the pituitary gland which are necessary for normal fertility. In view of the high affinity of the hypothalamic

hormones for their pituitary site of action, these antagonists should have the same high specificity of action and should thus probably be free of many of the unwanted side effects which are the major detrimental aspects of the present contraceptive agents. There is also reason to believe that antagonists of the hypothalamic hormones may be active as fertility control agents if administered only once a month rather than on a daily cycle as the present "pills."

At the moment the structure of only one of these brain hormones has been fully elucidated; indeed the substance was synthesized in 1969 and is already in clinical use. Having completed the isolation and the synthesis of the first of these brain hormones, our laboratory is now devoting its effort toward the isolation, characterization and synthesis of one or possibly two other brain hormones which are known to be the ultimate control of the function of the pituitary gland as it relates to the normal function of the reproductive organs, the ovaries, and the testes. I consider that this synthesis of the antagonist substances is a problem of primary significance in view of the practical implications for fertility control. Obviously, availability of a once-a-month medication suitable for many cultural groups, easy to administer, practically free of unwanted side effects, and manufactured at extremely small cost (in view of the simplicity of the molecules involved) would represent a powerful new tool for fertility control.

It took approximately fifteen years of fundamental research from 1955-1969 to go from the original conception of the existence of these brain hormones to the first isolation and synthesis of one of them. This research required utilization of the most advanced methodology presently available in physical chemistry as well as availability of several millions of fragments of sheep brain which were used to extract these extremely powerful substances. The sophisticated methodology necessary to conduct this research in terms of the physical chemistry, the biochemistry, and the physiology involved, requires a high level of research support.

The few laboratories in the United States most actively engaged in this field of research should be supported at a cost of approximately $1.5 million a year for at least five years. Probably $5 million a year will be necessary for three years to test and reduce to practice this new type of contraceptive agent.

"The immunological control of fertility is probable. Its advantages lie in the world-wide acceptance of immunologic procedures generally and in the likelihood that immunization programs could be delivered expeditiously."

SEYMOUR KATSH, PH.D.

Professor of Pharmacology
University of Colorado Medical Center
Denver, Colorado

Associate Dean for Graduate and
Research Affairs

IMMUNOLOGY AND FERTILITY CONTROL

If one analyzes the basis for the world's population problems, it will become immediately apparent that, among the many factors contributing to increased survival, immunological expertise has been of profound importance. If it were not for the progress made during the past half century in protecting man against communicable diseases by immunization, a considerably higher death rate would have occurred. It would, therefore, be more than an ironic twist to turn the single most effective method of preventing death on a mass scale into an effective method of controlling reproduction and, thereby, into preserving the quality of life. I refer to immunization programs for control of reproduction.

At this time, there is a wealth of information from studies in basic immunobiology indicating that there are specific antigens in sperm, in male accessory organs and in at least one female reproductive tissue (the trophoblast), let alone the possibilities of employing pituitary gonadotrophic

hormones, steroid hormones, prostaglandins, etc. as antigens.

This spectrum of antigens provides for a variety of approaches for control of reproduction from control of conception (prevention of fertilization of the ovum), to prevention of implantation, and induced abortion. In other words, the possibilities include every level of the reproductive process in the male or the female subject to immunologic intervention. What are the probabilities of attaining this goal? At this time it is known that infertility can be induced in male and female experimental animals. It is also known that a very small percentage of human males and females are infertile as a result of spontaneous immunologic reactions to reproductive antigens. It is, therefore, more than speculation to say that immunologic control of fertility is possible; it is probable. What are the advantages of such a method? Although many could be cited (such as the specificity of the reaction) the main advantages would lie in the world-wide acceptance of immunologic procedures generally and in the likelihood that immunization programs could be delivered expeditiously. Moreover, the effects could be of long duration or the effects could be reversible should that be desired.

How soon could we expect to employ immunologic procedures for control of fertility in humans? In part, the lag period is a function of money to assemble teams that could extract, purify and characterize the large number of antigens that might be employed and to design adjuvants that would be acceptable for human use. Such teams should include reproductive biologists, endocrinologists, biochemists, physical chemists, immunologists, protein chemists and pathologists working first at the level of laboratory experimental animals, then with sub-human primates and, finally, with humans.

How much should one budget for such a program? The answer depends, in part, upon how rapidly and urgently one requires answers. Calculating on a single team with the essential apparatus, appropriate animal facilities, etc., a conservative estimate would be $440,000 (not including laboratories) for the first year. Laboratory space would add $1 million to this figure. However, it would be more reasonable to establish a minimum of three such laboratories (laboratory animals, sub-human primates, and human investigations) for extraction, purification and characterization of antigens, antibody responses, etc. **Since efforts with primates are considerably more costly, at least $3 million per year for three laboratories is required for a minimum of five years.**

"The production of antibodies gives every evidence of suggesting new methods of fertility control."

CHOH HAO LI, M.D.

Director, The Hormone Research Laboratory
University of California
San Francisco, California

THE POTENTIAL OF ANTIBODIES IN FERTILITY CONTROL

The production of antibodies has been shown to be a valuable tool in the study of reproductive processes and gives every evidence of suggesting new methods of fertility control. It seems clear that this tool which may be termed "reproductive immunology" will find ever increasing use and its development should be appropriately supported and encouraged.

Thus far, we have studied the role of the pituitary gonadotropins in reproductive processes such as ovulation, spermatogenesis, and maintenance of pregnancy. In addition, it has been possible to employ immunological techniques to further characterize the pituitary gonadotropins with respect to their purity and the relationship of one species of gonadotropin to that of another.

There are two pituitary gonadotropins of importance with respect to the regulation of reproductive function. In addition to being required for the

development and maturation of ova in the female and spermatozoa in the male, one of these hormones is also intimately associated with the process of ovulation. Chemically, both are proteins which contain carbohydrate as part of the molecule. In addition, each is composed of two smaller, chemically dissimilar subunits which are held together by relatively weak non-chemical bonding forces. Methods which dissociate the subunits of a gonadotropin leads to biological inactivation. Primary structures of these two subunits have recently been elucidated.

The pituitary gonadotropins have been shown to be good antigens in that antibodies can be produced against them in the proper host animal (rabbit or guinea pig). These antibodies react uniquely and specifically with the hormone used as the antigen. As a result of this unique reaction exhibited between antibody and antigen several important consequences result.

First, since the antibody reacts specifically with the antigen, it can be used for exquisitely sensitive and accurate methods of measurement of the concentration of the gonadotropin in physiological fluids. This technique has been termed immunoassay, and its application allows the study of the dynamics of gonadotropin action with respect to secretion from the pituitary and the relationship of hormone levels in the circulation to physiological processes. Thus, immunoassay techniques showed beyond doubt that there was a peak in the circulating concentration of the one hormone prior to ovulation and procedures which inhibited the "surge" of this hormone also inhibited ovulation.

A second important use of antibodies raised against the gonadotropins has been as biological blocking or inhibiting agents. Injection of the specific antiserum containing antibodies will cause the neutralization of the antigen and thus allow the consequences of this single hormonal neutralization to be studied. In addition, it suggests a method of possible fertility control.

It is possible, for instance, that that specific antiserum against one hormone can be used to inhibit ovulation in humans. In addition to the gonadotropins, antisera can now also be prepared against the sex steroids and possibly be used to selectively neutralize the action of a steroid in either the process of ova maturation or spermatogenesis.

It is also theoretically possible to immunize females against spermatozoa. If this could be controlled and made reversible, yet another immunological method of fertility control is possible. It may also be possible to immunize males, such that only viable sperm production would be affected.

These are but a few of the practical and applied applications which can derive from the development of reproductive immunology as a tool in the control of fertility. **Such studies should be supported at the basic, applied and clinical levels in a minimum of five centers for full benefit to accrue from its potential at an estimated level of at least $10 million per year for a period of five years.**

"Studies of steroid production and metabolism are important as a prerequisite to new contraceptive development and for understanding existing methods."

C. WAYNE BARDIN, M.D.

Associate Professor of Medicine
The Milton S. Hershey Medical Center
Hershey, Pennsylvania

PRODUCTION AND METABOLISM OF SEX HORMONES

The functions of gonads, of reproductive tracts, and of organs with hormone-dependent enzyme systems are influenced by factors which regulate the blood levels of the individual sex steroids. In the past ten years, the study of androgens and estrogens in man has been greatly facilitated by advances in radiochemical and immuno-chemical techniques which have allowed precise quantification of these sex steroids in blood. Such studies have established many of the control mechanisms which determine the balance of these hormones in man. Androgen and estrogen levels in the blood are determined by their production and metabolic rates.

The production of sex steroids occurs in many sites in the body, including gonads, adrenals, and several non-endocrine tissues such as liver and skin. In view of the diverse origin of the sex steroids in blood, their production

can be regulated by a variety of agents including pituitary hormones, steroid hormones and drugs.

The blood levels of sex steroids are also influenced by the rates of steroid metabolism. Steroids are metabolized in a variety of tissues, either to biologically inactive products which are suitable for excretion from the body or to compounds which have biologic activities equal to or greater than the parent steroids. Metabolism can therefore diminish or potentiate hormonal activity.

The delineation of factors which maintain normal levels of androgens and estrogens in man is particularly relevant to population research. The importance of these studies is underscored by the fact that many of the currently used contraceptives achieve their effects by perturbing the naturally occurring balance of pituitary and gonadal hormones. Not only do contraceptive agents influence the production of sex steroids, but they also markedly affect the metabolism of protein and steroid hormones, lipids, and a variety of drugs. These latter effects may underlie many of the undesirable side effects of contraceptives.

Studies of steroid production and metabolism are important as a prerequisite to new contraceptive development. Continued study will provide a better understanding of the mechanism of action of existing contraceptive agents. This will allow selection of the smallest possible effective dose to avoid or reduce potential undesirable side effects. In addition, a better understanding of steroid production and metabolism will facilitate the development of effective and safe new methods of contraception.

Secondly, continued study of steroid metabolism will increase our knowledge of many of the poorly understood pharmacologic effects produced by continuous administration of currently used contraceptives over a long period of time. Contraceptive agents are administered to large groups of healthy women and produce subtle metabolic changes which are difficult to detect by tests currently available in clinical laboratories. The kinetic experimental approach used in the study of steroid metabolism can detect and quantify subtle metabolic changes which occur during contraceptive treatment. Although these studies are complex, their precision and sensitivity allow meaningful data to be gathered on relatively small groups of patients.

Funds to maintain approximately 30 centers with both clinical and basic laboratory facilities are required to carry out studies of contraceptive development and evaluation of the medical effects of existing contraceptives. For this purpose, approximately $4 million per year over the next five years is needed for realistic funding of studies on steroid production and metabolism in humans.

"Knowledge of human tubal physiology may provide new and unique methods of controlling conception."

JACK LIPPES, M.D.

Associate Professor of Gynecology-Obstetrics
State University of New York
Buffalo, New York

Inventor of the Lippes "Loop"

RESEARCH IN HUMAN TUBAL PHYSIOLOGY

Here in Buffalo we have been collecting and studying human tubal fluid for four years. Why? Because the fallopian tube is where conception takes place. Tubal fluid provides the nutrition and the energy for the earliest development of the embryo. Sperm themselves may receive substances from the tubal fluid which enable them to fertilize the egg. If we can interfere with any of these processes, we may control fertility.

Furthermore, the presence of a catheter in the fimbriated end of the tubes provides a way to study the muscular physiology of the tube. The effects of pharmacologic agents on tubal muscle as well as the normal tubal muscle physiology which exists during the different phases of the menstrual cycle can be elucidated.

Protein patterns in human tubal fluid are different from the protein patterns of human serum. They could be utilized as antigens and eventually lead toward

an immunologic method for the control of conception. Knowing the many enzymes and substrates which exist in the tubal fluid provides opportunities to interfere with the energy requirements of the developing ovum and thus may lead to a simple chemical means of controlling conception.

It is quite evident from previous investigations that in almost all mammalian species, the early embryos are limited in their capability to utilize substances from the tubal environment as well as when put into culture. For example, early mouse embryos (2-cell stage) can utilize pyruvate readily whereas they cannot use glucose or lactate. However, during subsequent stages of development they acquire this capability. Since the pre-implantation mammalian embryos remain in the fallopian tube for five to six days before they implant in the uterus, it would be important to investigate the changes in the tubal fluid composition in various phases of embryonic growth (2-cell, 4-cell, 8-cell and blastocysts) as well as during implantation. The effect of various steroids and chemical substances on the tubal fluid composition and subsequent changes in the embyro, may provide valuable knowledge regarding the development of a more natural contraceptive.

The specific aims of such research would be to:

1. develop a surgical technique which would allow the continuous collection of human tubal fluid and permit studies of the human tubal environment;
2. develop a surgical technique to differentially collect tubal fluid from different parts of the human oviduct;
3. develop special catheters for this research;
4. ascertain how much of human tubal fluid is transudate or exudate;
5. biochemically elucidate the composition of human oviductal fluid;
6. characterize the proteins and/or enzymes of human oviductal fluid;
7. elucidate human fallopian tube muscle physiology.

The investigation of human tubal fluid, involving 50 patients for 8 days at one institution, amounts to about $120,000 for the first year. **Because of the important potential of such research, support should be for 12 institutions for a cost of about $1.5 million per year over a five-year period.**

"It is essential to maintain and develop further all the facilities for primate research if we are to make substantial progress in the development of research in reproduction and new contraceptives."

LUIGI MASTROIANNI, JR., M.D.

Chairman, Dept. of Obstetrics and Gynecology
University of Pennsylvania School of Medicine
Philadelphia, Pennsylvania

THE REPRODUCTIVE TRACT IN PRIMATE RESEARCH

Reproductive biology has several dimensions. It involves a diversity of fields—anatomy, biochemistry, immunology, embryology, enzymology, physical chemistry, and more—all of which must be used if we are to learn how to modify reproductive processes.

In order to explore the events which lead to a successfully implanted pregnancy, investigators have used a variety of laboratory animals. The rabbit, rat, mouse, guinea pig and hamster are among the most popular. The ultimate purpose of these efforts is to develop methods of contraception, which could be applied to Homo sapiens. Yet, the processes under consideration differ among the various animal species and are often distinctly different from those which have been observed in the human. Direct experimentation in the human is generally unacceptable, largely because the events under consideration are

inaccessible without doing harm. Hence, even in the hands of the most imaginative investigators, research on human reproductive process cannot always be carried out. Herein lies the importance of the use of the subhuman primate in reproductive research.

In the monkey, as in man, ovulation occurs spontaneously, and can be assessed hormonally. Fertilization and early development can be assessed in the primate using modern biological techniques. Thus, the monkey offers substantial advantages in reproductive research and provides a realistic intermediary between the basic laboratory animal and the human being.

Over and above the importance of monkey species in basic biologic research, the monkey is important in the screening of potential agents for fertility control before application to the human. Such approaches, as the use of a Silastic implant for slow release of a contraceptive agent, the post-coital pill and the induction of menses in the presence of an early pregnancy, can be evaluated in the monkey preparatory to use in the human.

Primate research requires elaborate facilities and expertise for the care and maintenance of the animals. Know-how for this has been developed in seven National Primate Centers and in nine individual laboratories throughout the United States, all supported by the Animal Resource Program of the National Institutes of Health.

It is essential to maintain and develop further all the facilities for primate research if we are to make substantial progress in the development of research in reproduction and new contraceptives. A particularly pressing need in university-based facilities is salary support for investigators who are devoting their principal energy to research in primate and human reproduction.

An investment of $4.8 million per year for five years would assure continuity of effort in reproductive biology in the primate area—$2.3 million for the primate centers, and $2.5 million for the primate laboratories.

"Our current understanding of the regulation of reproduction is rudimentary indeed. The rhesus monkey serves as an excellent experimental model for human reproductive phenomena."

ERNST KNOBIL, M.D.

Chairman, Department of Physiology
University of Pittsburgh School of Medicine
Pittsburgh, Pennsylvania

Ciba Award, Endocrine Society

THE ENDOCRINE SYSTEM IN PRIMATE RESEARCH

My laboratory is engaged in fundamental investigations of the mechanisms which govern the menstrual cycle and pregnancy in primates. These mechanisms comprise an elaborate and complex control system which involves a dynamic interplay between the central nervous system, the pituitary gland, the ovary and the reproductive tract.

The brain produces substances, still ill defined, which signal the pituitary gland to secrete two hormones which reach the ovary by way of the blood stream. Their action on the ovary is to cause maturation of the egg and its release for fertilization. In addition, these pituitary hormones stimulate the secretion of the female sex hormones which, in turn, have two actions. One is to control the brain-pituitary system by way of complex negative and positive feed-back mechanisms. The other is to condition the reproductive tract

to subserve its proper functions during reproduction, be it the migration of spermatozoa or the development of the fertilized ovum in the uterus.

The major objective of our research program is to describe this control system quantitatively and in considerable detail. In order to do so, much remains to be learned about its components as well as its basic operation and considerable developmental work remains to be done in the necessary methodologies for measuring the substances involved. The ultimate goal of this effort, of course, is to achieve a better understanding of how the reproductive cycle works. Our current understanding of the regulation of reproduction is rudimentary indeed. A full comprehension of the sequence of functional events and their underlying mechanisms would expose the system to a multiplicity of rational approaches to contraception. Currently, these points of attack are few and almost entirely empirical with the consequent danger of unforeseen and perhaps dangerous side effects.

One of the difficulties associated with fundamental research in reproductive physiology is that wide differences exist between species in the manner with which the same ultimate biologic goals are reached. For this reason, findings obtained in many of the common laboratory animals cannot always be extrapolated to man. The rhesus monkey, however, is remarkably similar to the human in the reproductive realm and serves as an excellent experimental model for human reproductive phenomena.

Clearly, monkeys are more expensive than rats and mice and the budgets of laboratories engaged in primate research are correspondingly somewhat higher for any given operational size when measured in terms of personnel and research output.

The optimal operational budget for our own enterprise, which is a relatively modest one in terms of numbers of professional workers employed, should be approximately $400,000 per year, not counting the support of young trainees. If training costs are added, this figure should come to $550,000.

Setting up such a laboratory would require an initial investment of $1-2 million, on the average, depending on the size of the intended operation. Experience to date has strongly indicated that the large (and expensive) primate research institutes have been relatively unproductive while the smaller research enterprises have yielded most of the significant basic information directly applicable to fecundity control. Viewed in this light, the funding of a larger number of individual research groups of proven productivity is vastly more profitable than creating one or two large institutes *de novo*.

Ideally, there should be at least ten laboratories in the U.S. engaged in related neuro-endocrine research in primates. This would require an operational funding level of about $5.5 million per year for five years.

DEVELOPMENTS IN CONTRACEPTION

"The addition of copper or zinc to a plastic intrauterine device appears to be significantly better than the ordinary plastic IUD's in both effectiveness and decreased side effects."

DEAN L. MOYER, M.D.

Chief, Experimental Pathology
University of Southern California School of Medicine
Los Angeles, California

SECOND GENERATION IUD's

The development of an ideal contraceptive method requires that it have a high rate of effectiveness in preventing pregnancy and that the severity of the short and long term side effects be either minimized or nonexistent. To accomplish these goals research teams have chosen to modify the environment in the female reproductive tract by introducing medicinal substances directly into either the uterine or vaginal cavity. These medicines do not circulate throughout the body as a whole but remain in the reproductive tract.

One important contraceptive method utilizing medications in the female reproductive tract consists of the addition of a piece of metal to an intrauterine device. One of the most promising methods utilizes a small quantity of metal, usually copper or zinc, which is attached to an intrauterine device and placed within the intrauterine cavity. The addition of copper or zinc to a plastic intrauterine device appears to be significantly better than the ordinary plastic IUD's in both effectiveness and decreased side effects. It is believed that the

mode of action of a metal IUD operates by means of a different biological principle to inhibit fertility when compared to a conventional IUD. In the early studies, the continuation rate among women using the copper IUD was 95% to 98% compared to 70% to 80% for the conventional IUD in the same period.

Conventional IUD's have been studied extensively in human populations and domestic laboratory animals, and these investigations have taken close to ten years before an accurate assessment of the basic principles of action of the IUD were forthcoming. As with the conventional IUD's, basic investigations including the mode of action of copper IUD's should be performed in a number of university centers and medical schools throughout the world.

The budget requirements of a product-oriented program for development of copper IUD's will include the toxicological and teratological studies in large numbers of laboratory animals as well as clinical testing. About $1 million will be required for toxicological studies in experimental animals. Formulation of metal-containing intrauterine devices, cost of materials, supervision of the entire project of competent medical personnel and able administrators and the compilation of the necessary statistical material will require some additional funding. Extensive clinical studies will need to be performed requiring the study of approximately 10,000 women and between 100,000 to 200,000 cycles during at least a six year period. **The total costs will range somewhere around $1 million a year for at least six years to bring the metallic IUD to a stage where it will be considered to be safe and efficient.**

In the event that the copper IUD proves to be successful, other metals and compounds will need to be studied intensively. In the case of the copper IUD, cost estimates have been made excluding some of the initial development costs which had taken place prior to this writing. Starting from an earlier stage of development for other compounds, an additional $1 million may be added to the base cost for each compound. These costs include the development of biological models to test specific compounds. Therefore, for each compound which appears to be worthy of study after the initial testing phase, a total amount around $2 million appears to be a reasonable figure for development at today's cost. **If during the next ten years at least one metal other than copper is thoroughly studied and three to seven medicinal substances incorporated in plastic for intrauterine administration, then a conservative estimate for laboratory and clinical development of these methods of contraception may require at least $8 million for development per year.**

"Recent developments in the prostaglandin field have offered some promise that prostaglandins may have some value as a once-a-month fertility control agent. But an enormous amount of effort will be required if this class of drugs is to become acceptable for widespread use in population control."

CHARLES H. HENDRICKS, M.D.

Chairman, Department of Obstetrics
& Gynecology
University of North Carolina School
of Medicine
Chapel Hill, North Carolina

Foundation Prize, Association
of Obstetrics and Gynecology, 1956

PROSTAGLANDINS IN FERTILITY CONTROL

Our research group is studying the prostaglandins as possible fertility control agents. To date, utilizing the intravenous route, we have successfully induced premature labor with both prostaglandins E_2 and F_{2a}.

Recent developments in the prostaglandin field have offered some promise that one of the natural prostaglandins, or a prostaglandin analogue, may have some value as a once-a-month fertility control agent, as a means of regulating the menses, and as a method for inducing labor.

However, human studies, which have been underway only for the past eighteen months, indicate that we are still far from widespread clinical application of this particular class of drugs. The total world experience reported to date, using all types of prostaglandins and all routes of administration,

totals far less than 1,000 cases as of March 1971. Intravenous, intrauterine and intravaginal methods have all been tried, many accompanied by unacceptably high rates of complications and undesirably high rates of nausea, vomiting, and diarrhea.

An enormous amount of effort will be required if this class of drugs is to become acceptable for widespread use in population control. The optimal form of the drug must be identified and tested. The dosage range and rate of administration must be determined. Measures must be devised for minimizing complications and avoiding unpleasant side effects. Perhaps most important of all, much basic work remains to be done in determining the short-range and long-range biologic effects of this drug upon the human organism.

A number of people knowledgeable in this field believe that we are still about five years away from bringing any of the prostaglandins to full clinical use. If they are to be developed with maximum speed and safety, the cost in time and money will be very large. Nevertheless, in view of the urgency of our population problem, a major commitment devoted toward further development of the prostaglandins seems warranted.

I estimate that if we want productive development of prostaglandins, we can utilize profitably between $10 and $30 million a year for the next five years.

"A long-acting injection is probably the closest thing yet to a practical mass contraceptive agent; it is easily administered, long-acting, requires no continuous motivation, and is acceptable to women in many parts of the world."

EDWARD T. TYLER, M.D.

Associate Clinical Professor of Obstetrics and Gynecology
University of California School of Medicine, Los Angeles, California

President, Family Planning Association of the Americas
First President, American Association of Planned Parenthood Physicians, 1963-1965
Member, WHO Scientific Group on Oral Contraceptives, 1965-1966
Honorary Oliver Bird Lecturer, London, 1968
Member, Royal Academy of Medicine

LONG-ACTING INJECTABLE CONTRACEPTIVES

Experience has shown that pills that must be taken carefully according to a rigid routine are not a completely practical method of pregnancy control for many women, particularly in developing as well as in developed nations. Therefore, an injection which would interfere effectively with fertility for long periods of time was considered at a very early stage in the development of hormonal contraception.

One hormonal agent called medroyprogesterone acetate (MPA) had already been in use for nearly a decade in "depot" injectable form for various gynecological purposes. Its properties, including its ability to suppress ovulation for long periods of time, are well known. In our Los Angeles Family Planning Clinics, for example, we have had relatively good acceptance of various long-acting injectable contraceptives among about 1000 patients during the past decade. Other clinical studies in Chile, Brazil, Mexico, South Africa,

and many in the United States confirmed the acceptability of injections that lasted for one or three months.

Despite the well-known irregular bleeding pattern associated with the use of MPA, it was apparently the only successfully employed contraceptive for a group of our patients. Further, I am sure that in certain areas, particularly in the developing countries, where injections are looked upon as good preventive medicine, the availability of a long-acting injectable contraceptive is important. Finally, the more methods that we can make available to various cultures, the more likely it will be that we can make progress in controlling over-population.

For these reasons, I believe a long-acting injection is probably the closest thing yet to a practical mass contraceptive agent; it is easily administered, long-acting, requires no continuous motivation, and is acceptable to women in many parts of the world on the basis of results in clinical trials.

Since there are problems inherent, theoretically at least, in the use of long-acting progestogens alone, intensive metabolic studies are required. Also, there are rumors that the specific contraceptive use of MPA may be prohibited by the U.S. Food and Drug Administration, even as an experimental agent. At the same time, I know of no recent specific laboratory studies to indicate that MPA is toxic nor that any recent significant animal mammary experiments (other than studies with beagles) would lead to an adverse decision by the FDA. In general, long-acting injectable agents are probably not being developed by the pharmaceutical industry at the present time because drug company officials feel that ultimate approval is uncertain. Foreign drug companies have not been active, partly because they are not yet interested in "demographic" markets whose sources of funding are uncertain, and partly because they fear the worldwide impact of adverse FDA opinions.

It is difficult to estimate the total cost of research for developing a long-term injectable. If one were to try to develop a combination estrogen-progestogen injectable, there would be costly clinical pharmacology simply to obtain proper relative amounts for cycle control. **It is my judgment that, assuming one were required to develop new chemicals not already patented, this would be a very difficult project in itself. Add to this the necessary clinical pharmacology and adequate testing for effectiveness and safety, a realistic minimum research requirement might be in the range of $2.5 million per year for a minimum period of ten years.** The money would be well-spent if an easily-used, safe, injectable agent were developed, for there is a very definite place for this type of method in the pattern of international population control.

"There is a great need for dealing with the problem of developing appropriate contraceptive techniques for the male where our present-day knowledge is relatively primitive."

C. ALVIN PAULSEN, M.D.

Professor of Medicine
University of Washington School of Medicine
Seattle, Washington

DEVELOPING MALE CONTRACEPTIVES

The male reproductive system has two major responsibilities. One is to produce mature germ cells called spermatozoa; the second is to manufacture the potent sex hormone, testosterone. It is not generally appreciated that the controlling mechanisms for these processes have the same degree of complexity as do the mechanisms controlling the female reproductive system. Indeed, if viewed from the aspect of our present-day ability to induce a state of temporary sterility without harming other bodily functions, the male reproductive system presents a picture which is more complex in nature than that of the female.

To further appreciate the reasons for this situation, consider first, the transport mechanism. After the germ cells have matured in the testis they pass through a network of tubes or ducts which eventually lead to the outside via the urethral opening at the end of the penis. Interruption of this pathway can be achieved rather simply by either a mechanical device such as a condom

sheath or by performing a minor surgical procedure (vasectomy). The main problem in employing these techniques for controlling fertility is that the condom sheath lacks general acceptance while the vasectomy usually imparts permanent sterility.

Consider, second, germ cell and male sex hormone production. These two testicular functions are controlled by two separate hormones which emanate from the anterior pituitary gland, which is situated at the base of the brain. One of the pituitary hormones promotes germ cell maturation while the other promotes male sex hormone production. Although these two pituitary hormones receive stimulating signals from higher brain centers, the testis itself sends inhibitory signals to the pituitary gland that control the rate at which these two pituitary hormones are secreted into the blood stream, thereby affecting the testis. In other words, the pituitary-testicular axis operates under a negative feed-back mechanism.

Therefore, if the male sex hormone is produced in excessive amounts within the body or alternatively is administered to a man in sufficient quantities, the manufacture of the pituitary hormone which promotes male sex hormone production will decrease. By administering male hormone, the production of the other pituitary hormone which promotes germ cell maturation will also decrease and germ cell production will cease. If administration of sex hormone is stopped, the pituitary resumes function and germ cell production returns to normal. Although manipulation of the pituitary by administration of those amounts of sex hormones appears ideal for contraception, other bodily functions are altered. This results, for example, in an increase in certain proteins in blood responsible for transporting fat, which renders the use of natural or known synthetic male sex hormones by themselves impractical. A more precise means to stop germ cell production would be to administer that testicular substance which controls the pituitary hormone that is responsible for germ cell maturation. Unfortunately, the identity of this agent is not known, nor do we know exacly where in the testis it is manufactured. Clearly, more studies are required to solve this problem.

We need a strong commitment of ten years or more and adequate financial support if we want to attract the necessary numbers of promising young scientists to join us in solving these problems. This need is great, particularly in dealing with the problem of developing appropriate contraceptive techniques for the male where our present-day knowledge is relatively primitive. **I estimate adequate financial support in this area would require the expenditure of $25 million per year for a five-year period.**

"We are obliged to support efforts to develop better, safer and more attractive methods of sterilization for the responsible couple with the completed family."

J. F. HULKA, M.D.

Associate Director
The Carolina Population Center
University of North Carolina
Chapel Hill, North Carolina

THE DEVELOPMENT OF IMPROVED STERILIZATION METHODS

Average married couples achieve their desired family size early in their reproductive years. They then face about a 20-year "risk period" during which they must practice highly effective birth control if they are to avoid unwanted pregnancies. The pill and the IUD at best are about 99% effective. If 100 couples relied on these methods for the 20 reproductive years after completing their family, calculations have revealed that 30 of them would have more pregnancies than planned over this long risk period. Taking a hormone almost daily for 20 years seems medically radical to some doctors and to many patients. Most couples try the pill or IUD for a few months or years, then abandon them for less effective methods: condoms, foam, rhythm, etc. If we generously call these methods 95% effective, calculations reveal that 80 out of 100 such couples would have unwanted pregnancies before the woman reaches menopause.

With the recent emerging sense of responsibility toward reproduction on the part of both men and women, more couples are reaching the conclusion that they do not wish to risk further pregnancies by relying on currently available contraceptives, and are asking to be sterilized. We are obliged to support efforts to develop better, safer and more attractive methods of sterilization for the responsible couple with the completed family.

For the male, vasectomy is a simple office procedure. Even so, such operations were accepted by only 40,000 fathers annually in the 1960's, or about one for every 100 babies born. Recently, family planning clinics and urologists have experienced a sharp increase in requests for vasectomy, together with inquiries as to reversibility.

Studies in several centers are currently underway to develop more reversible methods of male sterilization. These studies involve unexplored problems in male reproductive physiology and bioengineering (valves, intravas devices, clamps, shunts, frozen sperm, etc.).

Women have also recently demonstrated growing interest in sterilization. In the 1960's sterilization of women required general anesthesia, major surgery, and at least four days' hospitalization before and after surgery. Nevertheless, over 100,000 mothers (or about three for every 100 babies born) elected this method annually. In 1970 clinics and gynecologists have experienced increases in requests for sterilization procedures, again usually with inquiries as to reversibility. Standard "post partum tubal ligation", when freely offered, is now being accepted by ten to fifteen out of every 100 women who have just delivered a child. When offered to women with completed families undergoing abortion, sterilization is accepted by almost half. If the techniques were simpler and safer (and perhaps more reversible), undoubtedly even more women would accept this method of limiting their family size.

Recent research in bioengineering technology has achieved a modest clinical breakthrough for some contraceptors who want a permanent method of birth control. In clinics in Europe and North America, non-pregnant women are undergoing laparoscopy or colpotomy: small openings through the abdominal wall or vaginal canal allow special instruments to locate, clip or cauterize the tubes. These procedures have been attractive to thousands of women because they involve no large scar and require only 12 to 24 hours away from the husband and children. However, these procedures are technically complex and expensive.

Research is currently underway to find simpler and cheaper methods more suitable for female sterilization. Studies of other simple sterilization methods as office procedures have been carried out sporadically in the past and are currently proposed by several research centers. Among these methods are cautery, freezing, biologic adhesives, etc.

Current estimates from leading scientists and research institutions call for an annual expenditure of around $5 million, divided equally between studies of male and female sterilization for at least five years.

"Research for the improvement of the rhythm method is difficult to pinpoint directly because it subsumes research in all areas of fundamental reproductive biology."

ANDRE E. HELLEGERS, M.D.

Professor of Obstetrics and Gynecology
Georgetown University
Washington, D.C.

Member and Deputy Secretary-General,
Pope Paul's Commission on Population
and Birth Control, 1964-1966
Member, President's Commission on
Population and Family Planning, 1968
President, Perinatal Research Society, 1971

RESEARCH ON THE RHYTHM METHOD

The rhythm method of family planning is the only method acceptable to a sizable fraction of the American population. Specific research for the improvement of the rhythm method is difficult to pinpoint directly because it subsumes research in all areas of fundamental reproductive biology which leads to the development of better contraceptive methods with the rhythm system being the incidental beneficiary.

The essence of the rhythm system depends on placing acts of intercourse at such times that surviving sperm and ova never meet.

The fundamental biological questions to be answered in rhythm research are the following:

1. How long can sperm survive and what determines the survival period? Does this vary with age of the person? Does this vary from person to person? Does it vary with physiological variables in the vagina, cervix, uterus and

fallopian tube of the particular woman?

2. What determines the onset of ovulation? How long can an ovum survive and be fertilized? Does this vary from woman to woman?

3. Since the fundamental essence of the rhythm system is having intercourse as far as possible from the time of the single ovulation, it must follow that if fertilization results, it will occur either with an ovum which is at the end of its life span, or with sperm which are at the end of their life span. Does fertilization with such "old" gametes lead to normal or abnormal pregnancy outcome?

4. What tests can be developed to determine: whether ovulation has occurred; whether the ovum has survived; and the time of ovulation several days in advance so that no sperm shall be deposited whose survival time could lead to fertilization?

Since the perfection of the rhythm system subsumes a total knowledge of the processes of fertilization, it is impossible to place a separate price tag on rhythm by itself.

In practice, when such basic knowledge has been achieved (and it could be gathered by those interested in the production of artificial contraceptives as well as those interested in rhythm) it will then demand a phase of development in which the critical symptoms and signs of sperm and ovum life can be monitored by methods which can be taught to anyone.

At present, no monitoring method for sperm survival is available. The only reliable monitoring method for the occurrence of ovulation is the thermometer. While many can be taught to take their own temperature, the process is found to be tedious, open to error, and the logistics of teaching prohibits use on a mass scale. There is, therefore, an early need to develop easier methods of temperature recording. With the vast increase in knowledge in telemetering systems by American industry, adequate funds could lead to the development of methods to determine a method of temperature change at ovulation which would be available and teachable on a mass scale. Methods of this type are already well into a phase of development and only a lack of research funds prevents their further development.

It is estimated that adequate and easier monitoring methods will require national funding levels of around $2 million for at least five years.

"Extensive study is required in order to develop adequate experimental bases for ascertaining both effectiveness and safety in anticipation of clinical use of recently developed contraceptive agents."

ROY HERTZ, M.D.

Associate Director
The Population Council
New York, New York

RESEARCH ON HEALTH ASPECTS OF CONTRACEPTIVE AGENTS

Historical review clearly indicates that most of our current public health practices were initiated by voluntary agencies and gradually became official functions of local or state governments. Examples of this progression are tuberculosis control, venereal disease prevention, and mass immunization against poliomyelitis and other communicable diseases. Although our society is just approaching a consensus as to the desirability of population limitation, we are just now developing both our criteria for the definition of "unwanted pregnancy" and our methodology for combating it.

In developing any preventive or therapeutic procedure, two ancient requirements apply: (a) Primum non nocere (above all, do not harm) and (b) the most feasibly accurate determination of the ratio of the risk taken to the benefit to be obtained. These are principles which are very difficult to define

in universally applicable terms. The best we can do is to try to reach some sort of consensus as to what is acceptable under prevailing conditions. The least we can do is to marshal as comprehensive a body of fact as possible to provide a basis for our evaluations.

One key issue in such evaluation is effectiveness. Considerable progress has been made in developing criteria for effectiveness both from an individual as well as from a demographic point of view and there has emerged a substantial degree of know-how in this area.

Another key in such evaluation is safety. In contrast to the problem of effectiveness, the problem of safety still calls for ground breaking effort. Major difficulties arise in three areas: (1) rare events which can be assessed only from experience in large scale, well controlled studies, (2) long-term or delayed effects demanding prolonged follow-up and continuity of observation, and (3) largely subjective effects which vary widely in differing population groups.

Growing appreciation of the enormous impact of economic, social, cultural, and genetic factors leads one to demand a high degree of control in the design of studies aimed at determination of all of these effects. Only properly designed, well controlled, long-term observations on statistically adequate numbers of people can provide useful information.

It is generally agreed that prior animal studies can be helpful in some cases. Accordingly, animal data are widely used in detecting potentially effective agents and in determining their probable safety. However, such observations have so far served to exclude certain contraceptive agents from use rather than to insure against harm from those still in use. Extensive study is required in order to develop adequate experimental bases for ascertaining both effectiveness and safety in anticipation of clinical use of recently developed contraceptive agents.

It may be impracticable to estimate the probable costs of clearly indicated undertakings in this area because the required information has such basic importance for so many of us that no cost should be spared in underwriting any soundly devised study which will provide a scientific basis for this newly emerging segment of public health practice. **It is estimated that a reasonable level to permit productive development and significant results in this field is in the range of $2-5 million a year for at least five years.**

"In spite of prolonged experience, the specific, detailed and systematic assessments of contraceptive methods in the human have been quite variable and inconclusive."

CELSO-RAMON GARCIA, M.D.

Director, Division of Human Reproduction
University of Pennsylvania School of Medicine
Philadelphia, Pennsylvania

Carl Hartman Award, 1961

ASSESSMENT OF CONTRACEPTIVE METHODS IN HUMANS

There is wide agreement on the need to develop a variety of contraceptive means since it is apparent that no single method can be universally acceptable. Basic science has evolved and is developing a profound understanding of approaches or effects through which the reproductive processes can be altered to reduce or prevent unwanted births. Projecting on these findings, efforts are being directed toward development of new contraceptive techniques.

The oral contraceptives have emphasized the utter need for detailed and continuing monitoring of effects even after initial acceptance. While initial review and screening for safety in sub-primate species is essential, a greater need for review in sub-human primates is being realized. But animal studies cannot be a substitute for human evaluation.

In spite of prolonged experience, the specific, detailed and systematic assess-

ments of contraceptive methods in the human have been quite variable and inconclusive. The need to systematize and coordinate these is apparent. Centers for such human evaluation are urgently needed. Careful supervision of large patient populations with a variety of contraceptive methods permitting the evaluation of newer approaches are needed not only to evaluate contraceptive efficacy in new and improved versions but also to assess potential side effects and focus attention on the detailed evaluation of their metabolic and physiologic effects.

Such centers ideally should have reproductive biology capabilities to include sub-human primate colonies complemented by human clinical facilities. They should have firm support from the clinical laboratories in the area of physiologic chemistry, hematology, radiology, neurology and endocrinology. Thus, the effects on the cardiovascular, respiratory, renal, hepatic, neurological and gastrointestinal systems as well as those possibly altering the endocrine and reproductive systems should be available. Psychological testing should also be provided to attempt objective review of emotional and motivational effects. The coordination of such activities would also require a facility for data recording, retrieval and analysis.

The major effort of these activities should allow for a patient population among whom a selected orderly review of the above could be carried out. This permits enhancement of the total patient care. It must be emphasized that routine care and specific studies have heretofore been separated. With increasing frequency it is becoming apparent that these are one and the same.

Specific guidelines must be developed for consistent, detailed and prolonged follow-up with a linkage between smaller clinical centers in the major cities of the United States. About ten major population research centers of this calibre should be established regionally and smaller clinical centers added and integrated into the larger network.

By selecting those areas where primate facilities are presently engaged in reproductive research and where clinical facilities are likewise functioning, some three or four population centers could be established almost immediately.

I estimate that ten major population research centers would cost $5 million per year, and as a group the smaller clinical centers would cost $5 million per year, for a total cost of $10 million annually over an initial six years.

SOCIAL RESEARCH

"A rational population program requires the involvement of a multidisciplinary fraternity of economists, psychologists, political scientists, and lawyers—a group which is now only peripherally concerned with population problems and which has an enormous unused resource of talent."

FORREST E. LINDER, PH.D.

Professor of Biostatistics
School of Public Health
University of North Carolina
Chapel Hill, North Carolina

Chief, Demographic and Social Statistics, United Nations, 1947-1957
Director, National Health Survey, U.S. Public Health Services, 1957-1960
Director of U.S. National Center for Health Statistics, 1960-1967
Bronfman Prize, American Public Health Association, 1967

RESEARCH IN BEHAVIORAL SCIENCES RELATED TO POPULATION

With a background of over three decades of professional work in the U.S. Census Bureau, the Statistical Office of the United Nations, and as the first Director of the U.S. National Center for Health Statistics, I am acutely aware that general research in the area of U.S. fertility statistics is one of the most neglected aspects of the U.S. statistical organization. The U.S. needs a new statistical system focused on the fertility characteristics of the American population.

A precondition to the design of a data base to serve the emerging needs is a variety of methodological investigations and a continuous and parallel series of studies on the attitudes and fertility characteristics of the population. These studies should cover four broad areas of investigation:

1. Measurement of population change. Under international aid financing

there have now been established three Laboratories for Population Measurement in three continents. Unfortunately there have not been sources or funds for a U.S. Laboratory which could act as a prototype for advanced methods for this international effort. In general, research in measurement methods should focus on problems unique to the population change problem, such as the development of pregnancy and abortion prevalence studies, family planning surveys, population growth surveys, methods for determining factors related to the rapid growth of the number of U.S. illegitimate births, causes underlying migration trends that create urban congestion, etc.

2. Effects of government policies affecting population. Many government policies, whether it is their intended purpose or not, have a significant influence on population change. The existing policies having such influences should be identified and evaluated and new policies which may influence population change in accordance with national objectives should be formulated and their possible impacts carefully appraised. Such policies may relate to various negative or positive incentives for fertility modulation. The effect of possible incentives of these kinds is at present very poorly understood, and yet many governmental programs costing hundreds of millions of dollars are having an unrecognized effect in one direction or another.

3. Social, economic, and psychological factors affecting population change. A rational population policy and program must obviously take cognizance of such elements as the social, economic, and personal factors influencing desired family size and elements affecting success in achieving that desired size. Closely related to this are elements determining concepts on family structure, values governing sexual relations outside marriage, illegitimate births, etc.

4. Consequences of population change. There are numerous major questions about population growth to which answers must be found before a solid U.S. population policy can be established. For example: What are the social, economic, and environmental consequences of population growth? What are the components of the GNP that may have a negative value as population increases? What are the effects of a slowing of population growth and the consequent change in population-age structure?

The issues indicated above require the involvement of a multidisciplinary fraternity of economists, psychologists, political scientists, lawyers, etc.—a group which is now only peripherally concerned with population problems and which has an enormous unused resource of talent that could be directed to this matter.

This program of the field research would require around $4.5 million in 1971 and rise to the level of $35 million by 1976.

"At this juncture of the history of this nation, it would be penny-wise and pound-foolish not to conduct the badly needed research to eliminate the various aspects of the urban crisis."

PHILIP M. HAUSER, PH.D.

Director
University of Chicago Population Research Center
Chicago, Illinois

U.S. Representative, Population Commission, United Nations, 1947-1951
President, Population Association of America, 1951
President, American Statistical Association, 1962
President, American Sociological Association, 1967-1968

RESEARCH ON POPULATION DISTRIBUTION AND URBANIZATION

The United States is, perhaps, the world's most dramatic example both of the population explosion and the population implosion. The former refers to the remarkable rate of population growth which has transformed this nation from a small isolated country of fewer than four million in 1790 to one of the two major world powers, with a population of 205 million in 1970. The population implosion refers to the increased concentration of population which has transformed this nation from an agrarian society—95% rural in 1790—to an urbanized and metropolitanized society—74% urban and 69% metropolitan—in 1970.

The urban crisis which confronts this nation may be better understood when it is realized that the year of the 19th Decennial Census, 1970, marked the completion of the first half century of this nation as an urban nation.

The urban crisis encapsulates many problems, environmental, physical, personal, social, economic and governmental. Although a large number of programs have been mounted to deal with urban problems, there is yet to be developed a comprehensive, systematic approach to the resolution of these problems. A prerequisite to such an approach is a sound foundation of facts based on research which is just beginning to accumulate. Increased research is needed on the following:

1) At what point in growth of urban and metropolitan areas may the nation be experiencing diseconomies of scale?

2) What can be the role of "new towns" in effecting a better distribution of population?

3) Why are more than half the counties of the nation continuing to lose population while metropolitan areas become increasingly congested?

4) What are the implications of the emergent megalopolitization of the nation?

5) What are the implications of the increasing separation of whites and blacks in metropolitan areas with blacks concentrated in central cities and whites in suburbs?

6) To what extent have public schools kept up with the need of urban populations, especially those in inner zones of central cities?

7) What has been the impact of Federal housing programs on the quantity and quality of housing throughout metropolitan areas and on the distribution of population by race, ethnicity, income and socioeconomic status within metropolitan areas?

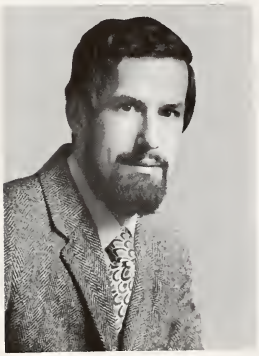
8) What is the trend with respect to the concentration of the "poor" and minority groups within metropolitan areas?

9) To what extent has the urban plant, including residential areas, retail and service trades and industry, responded to the implications of 20th century technology and its potential?

These are but a few problems which need investigation if the United States is to achieve an integrated policy and an holistic approach to the resolution of the urban crisis.

At this juncture of the history of this nation, it would be penny-wise and pound-foolish not to conduct the badly needed research to eliminate the various aspects of the urban crisis. To provide the funds for the proposed types of research outlined would provide the nation with one of the highest rates of return on its investment. **I estimate that research on population distribution and urbanization would require around $2 to $4 million per year for a minimum of five years.**

"The best research minds in economics, psychology, sociology, and management are needed if these basic and applied research problems are to be resolved and population policies are to be scientifically founded."



T. PAUL SCHULTZ, PH.D.

Director, Population Research
The Rand Corporation
Santa Monica, California

THE ECONOMICS OF POPULATION POLICY: A NEGLECTED FIELD OF PRIORITY RESEARCH

Rapid population growth in the world today is certainly in part a consequence of our unperfected methods of birth control, but this technological shortcoming is less important than is often assumed. Fundamentally, the problem is social; parents want more children than are needed to replace themselves. In this context the behavioral sciences have the critical assignment of improving our understanding of parents' motivations in having children. This knowledge is essential if we are to disseminate new birth control techniques effectively and if we are to choose wisely policies that promote a balance between social and individual welfare objectives while slowing population growth.

It is high time the effectiveness of various approaches to family planning were reckoned and only the most productive pursued. However, to infer with

confidence how much family planning activities have reduced the number of "unwanted" births, we must first have a basis for predicting the level of birth rates in the absence of program activities. What is required, therefore, is a comprehensive theory of the principal determinants of fertility.

Three major opportunities for policy to affect reproductive motivations have thus far been identified. The first set of policies strengthens the child's position in the family by compelling school attendance and prohibiting his early labor force participation, thereby forcing parents to invest more heavily in the future of each of their offspring. The second opportunity is associated with increasing the woman's economic opportunities to perform functions that are competitive with child-bearing. The third opportunity is to reduce infant and child mortality and thereby reduce the number of births required to provide parents with their desired number of surviving offspring.

An important task for empirical research is to confirm that public policies can accomplish these changes. The contribution of direct and indirect population policies must be documented, and their side effects, both good and bad, assessed. This information should enable society to make an intelligent choice of policies that most equitably narrow the apparent divergence between private and social interest in having children.

The best research minds in economics, psychology, sociology, and management are needed if these basic and applied research problems are to be resolved and population policies are to be scientifically founded. Unfortunately social science research can rarely be broken down into a list of separable and tractable tasks and assigned to teams of experts scattered across the research community. That approach appears more apt to the task of landing on the moon than to understanding the complex interactions that characterize society and man. In the social sciences each researcher must cope in some manner with the full complexity of the social system if his particular investigation is to be valid. Since there is not one best approach to understanding the determinants of fertility, a hedging strategy that supports research based on contending viewpoints is appropriate. For this reason research support should emanate from a variety of agencies; duplication may be less costly than would the foreclosure of options at this critical juncture.

The initial emphasis should be on developing and refining a theoretical and statistical framework and then applying it to the design of information systems that will facilitate policy evaluation and better management of family planning programs and other indirect population policies. **Less than two percent of the Federal population research budget, about $1 million, is currently being spent on economic and management studies of these issues. I think that amount could productively be increased by 1975 to $8 million.**

"Despite all the fine statements by world and national leaders about the importance of population problems, funds for research on human reproduction and natality control remain a trickle."

LESLIE CORSA, JR., M.D.

Director, Center for Population Planning
University of Michigan
Ann Arbor, Michigan

APPLIED FIELD RESEARCH FOR POPULATION PLANNING

Population planning, the application of knowledge in organized efforts to achieve optimal balance between human reproduction and quality of life, is one of the newest and most challenging areas of applied science. Being new, it attempts to draw upon existing knowledge from all relevant fields at the same time that it develops new knowledge within its own field. It depends upon shifting the specific interests of many basic scientists from long-term traditionally safe areas to the new controversial problems of the determinants and control of natality, and upon attracting young people's interests and skills to careers in the field. Money is one of the essential ingredients that make these changes possible.

Despite all the fine statements by world and national leaders about the importance of population problems, funds for research on human reproduction

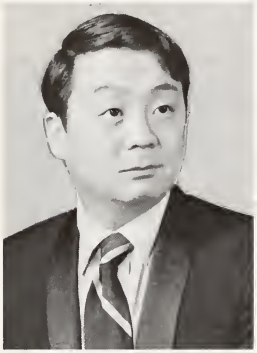
and natality control remain a trickle compared to those available for studying disease and mortality control. Funds for the development of university and other resources, essential both to seek new knowledge and to train research scientists in this new field, are pitifully scarce. If the rational use of man's intellect is to have an effect upon controlling the world's population growth for mankind's benefit, we are clearly spending far too little on making it possible and desirable for our brightest young people to prepare for research careers in population planning.

Essentially applied field research of all kinds contributes directly to our understanding of the causes and consequences of natality and to our ability to control natality rationally at levels compatible with the highest quality of life for the most people. This means seeking and testing methods in real life to reduce natality worldwide at present and, eventually, to maintain natality worldwide at whatever population size and densities seem optimal. Since family planning methods are a major final common pathway, the application and field testing of new, better methods are essential.

Since application depends upon the organizational ability of government and private institutions to make the best technology easily accessible and usable, it requires study of program acceptability by the people and by their leaders, and it requires considerable operational research on how best to achieve program goals. It involves research on motivation and on educational and economic incentive approaches, reexamination of the functions of women in various societies and research on how changes in those functions affect natality; and development and testing of new ways to provide basic security to parents in old age who now rely on their sons for such security. It includes research leading to a much better understanding of the complex contributions of natality to urban and other environmental problems, to employment, to recreation, to restrictions of personal freedoms, to rising costs of government that follow inevitably with increasing population density on those finite areas of earth most conducive to support human activities.

The magnitude and long-range import of these issues warrant much greater research investments as effective resources become available. **My judgment is that for the next five years, investments of the order of $25 million per year are needed to develop applied research resources, with emphasis on new manpower and training programs for them. An additional $50 million per year could easily be well used to enable present research scientists to shift their interests and work from other problems to applied population and natality issues.**

"Major breakthroughs in terms of concrete benefits do not come easily in the social sciences."



WILLIAM T. LIU, PH.D.

Director, Institute for the Study of Population and Social Change
University of Notre Dame
South Bend, Indiana

RESEARCH IN POPULATION DYNAMICS AND FAMILY WELFARE

Until only a few years ago, research on reproductive behavior, including marriage, conception, spacing, and fertility patterns, was done by a rather small but well qualified group of demographers. During the 1960's, social science research expanded to include sociology of medicine, family sociology, motivational and communication research, teen-age and child socialization, and social and economic change, especially as these related to population problems. This expansion of social science research into demographically relevant topics stemmed partly from the need for developing theories of fertility behavior, and partly from the requirement for multidisciplinary approaches to the problem of effective planning and usage of family planning clinics.

However, the growth pattern is uneven in terms of various traditional social science disciplines. Fertility studies based on the large scale sample survey

method is receiving more attention, whereas psychological research is underrepresented. Cost analysis and evaluation of family planning programs follow logically the expansion of governmental and private family planning clinics and health facilities. Along with the evaluation studies has been the refinement of measurements and usage projection studies, including the utilization of computer simulations. Along with the concern with fertility, is the concern with family health patterns, especially mortality rates due to chronic illness. These cumulative works have made enormous strides in the field of population research and family welfare.

The 1960's represented a rather exciting period for more imaginative kinds of social research, particularly with respect to family life. These works used variables not ordinarily handled by demographers in the past. For example, Freedman and Coombs used child spacing as an independent variable to assess the economic status of families in Detroit. There have also been some efforts to survey various primitive and pre-industrial societies with respect to the patterns of sex, childbirths, and fertility patterns by anthropologists based on ethnographic materials. Some empirical works, underway during the latter part of the 60's, dealt with the relationships between family structure and family size.

The field of social science is too broad and fertility behavior too complex to warrant a strict limitation as to what is immediately related to the population phenomenon. Social science research is further compounded by the divergent research designs and problems of quantitative versus qualitative measurement. Hence, major breakthroughs in terms of concrete benefits do not come easily in the social sciences. To estimate the cost and project needs in fiscal terms, therefore, would have to be general and even hazardous.

I estimate that the research needs require that 20 centers eventually should be supported. If graduate training, basic and applied research, and the center support programs continue according to the current thinking, a range of $40 to $60 million for social science research would be needed by the year 1975.

TRAINING AND ORGANIZATION

"The needed population research simply cannot be done by the existing body of skilled workers, but requires a substantial amount of training."

PAUL A. HARPER, M.D.

Professor, Population Dynamics
Johns Hopkins University
Baltimore, Maryland

TRAINING FOR POPULATION RESEARCH

Training of research workers is an essential and vital part of the government program of population research as laid down by Congress and signed by the President in Public Law 91-572, known as the Family Planning Services and Population Research Act of 1971. Sec. 1004 of that law recognized this as follows: "The Secretary/of Health, Education and Welfare/is authorized to make grants and to enter into contracts . . . for projects for research and research training. . ."

Others have written and testified eloquently as to the great importance of increased support for population research. The needed population research simply cannot be done by the existing body of skilled workers, but requires a substantial amount of training. Fortunately, research and research training go hand in hand; each supports and supplements the other.

There are three independent sources of the annual output of trained research workers needed to implement an expanded program of population research.

One source includes demographers-social scientists. A second source involves reproductive biologists. The third source covers a miscellaneous group of others, including post-doctoral training of physicians, lawyers, urban planners and educators. In the case of physicians, the average duration of training is two years. In all other cases, training for research averages nearly three years per person.

I estimate that for the next five years we will need an annual output of 185 research workers: 75 demographers-social scientists, 75 reproductive biologists and 35 others. If we allow 15 percent as the attrition rate for the annual number of workers admitted to training, then this will require a total of 600 man-years of training each year for the next five years.

The capacity is already present to train the demographers, largely in university departments of sociology. The training capacity in reproductive biology is substantial largely in the bio-medical centers and will be increased by new support for research. The capacity to train the others is now present in eight to nine selected schools of public health.

An allocation of 15 to 20 percent of research funds to support trainees who themselves will be assisting in research would seem to be a reasonable and wise allocation of resources. **My estimate of needed funds for research training for 1971 is $6 million and rises to $10 million by 1973.** These estimates are fully compatible with the additional funds for research authorized by the Family Planning Services and Population Research Act of 1971 (Public Law 91-572).

"No self-respecting business corporation would launch a multi-million dollar sale of an entirely new product among a strange clientele without market research."

SAMUEL M. WISHIK, M.D.

Director, Division for Program Development and Evaluation
International Institute for the Study of Human Reproduction
Columbia University
New York, New York

OPERATIONS RESEARCH: A MARKETING ORIENTATION

Family planning and population are today's concerns. People who need contraceptive services need them now and present program omissions and deficiencies contribute to future population growth.

Unfortunately, solutions are not as clear as the problems. Although it is true that rising standards of living and educational levels will usually result in time in lower average family size, there are few dramatic community or national demonstrations of acceleration of that process through organized program intervention. The matter involves people making changes in basic values and in their habitual interpersonal relationships. Answers need to be found that will make the programs more effective and more efficient. These answers must be sought through realistic trial and analysis of the services themselves.

No community or nation has a plethora of funds, facilities, or personnel. Nor would it be socially economical for professional health and educational workers to be diverted from other activities to take on new family planning functions. As has been recognized in other fields of public service, ways must be found to utilize auxiliary personnel. Duties must be delineated and information obtained on most appropriate methods of recruitment, training and supervision. This alone might repay the total investment in family planning operational research.

Most family planning services are built into the existing health infrastructure. It is important that ways be found whereby such integration can be most advantageous to the family planning services and least detrimental to the host health program.

Population groups who are in need of family planning services but remain apathetic toward them, require more effective methods of communication and motivation and messages identified that are relevant to their interests and needs. Special approaches may also have to be designed to meet the particular needs of certain subgroups, when barriers to effective communication exist because of language, marital status or other reasons.

It is essential that program settings not be restricted to those that have become traditional but that imaginative new outlets be sought. Similarly, persons involved in the investigations should be culled from a broad range of disciplines, not merely from the health professions. Implications in psychology, sociology, and business administration, among others, need to be considered and funds made available to attract to this work persons in those disciplines who have previously not seen this as a place for their contributions.

No self-respecting business corporation would launch a multi-million dollar sale of an entirely new product among a strange clientele without market research. Unfortunately, even though research is not done, family planning programs will be conducted and will be expanded. Money will be spent, but less wisely, less efficiently, and less effectively than should be the case; and the process will establish fixed procedures and new methods again resistant to the changes that may ultimately be recognized as needed. This can only be overcome by effective operations research.

For increased effectiveness and efficiency, we need about 50 different service programs to participate in studies of their activities and about 30 research groups for the scientific input. **With 50 studies going on in any given year at an average budget of $50,000, this would require $2.5 million a year. In addition, special competence should be institutionalized for organized conceptualization, investigation and dissemination in at least ten places, each involving field agencies in collaboration with research institutions. Each of these should be subsidized for at least $1 million for a total of $10 million a year.**

"The achievement of the national family planning goal can only be accomplished through a substantial expansion of operational research, program planning and evaluation studies."

FREDERICK S. JAFFE

Director
Center for Family Planning Program Development
Planned Parenthood/World Population
New York, New York

OPERATIONS RESEARCH: A PROGRAM

The President, in his 1969 Message on Population, and the Congress, in enacting PL 91-572, established as a national goal the provisions of modern family planning services within the next five years to all Americans who want and need them. This requires the development of an efficient delivery system, drawing to the maximum extent possible on existing health institutions but altering their programs to encompass family planning services and complementing them, where necessary, with new agencies. The achievement of the nation's service goal can only be accomplished through a substantial expansion of operational research, program planning and evaluation studies.

These investigations must provide information which will determine the size and nature of the program and improve its efficiency and effectiveness. The studies range from methods of estimating the number and characteristics of individuals in need of services to evaluation of different means of delivering services to various subgroups of the target population. The results of such

studies need to be embodied in detailed local, state and national plans for service networks and for the rational allocation of the fiscal and manpower resources.

Much of the operational research which has been done in family planning has been concerned with the growth of programs overseas. Few U.S. family planning research institutions or university population centers have devoted systematic attention to the domestic program. There is not in being a large cadre of researchers, program planners and evaluators with experience in dealing with the complexities of the U.S. program which operates through a pluralistic, multi-agency health system. To carry out the sophisticated research and evaluation studies required, it will be necessary to develop a number of institutions which are committed to systematic study of the U.S. program. The principal requirement is that they bring together a group of investigators from many disciplines who will commit themselves to long-term work in the areas of operational research, planning and evaluation on the domestic program.

The creation of five such R & D centers which concentrate on the domestic family planning program would seem to be a bare minimum. Each would need basic core support of at least $1 million annually (in addition to other funds for specific projects). At the present time, there is little support available from private foundations for domestically-oriented institutions and the Federal effort has lagged. A program to provide core support for such centers, with a commitment continuing over three to five years, seems essential.

In 1969, a committee of experienced researchers and administrators, convened by the Center for Population Research, attempted to project the financial requirements for an adequate five-year program in operational research, program planning and evaluation. The estimates they arrived at covered the costs of studies in Planning and Development, the Service Network and Delivery System, Communications and Education, and Evaluation. **Their cost estimates indicate that operational research requires funds to increase from $7 million in 1970 to $25.3 million in 1974.**

The cost of reaching the national service goal by FY 1975 is now grossly estimated at $350-400 million. Thus the estimates above would represent an expenditure for operational research, planning and evaluation of about 5-6% of program costs. This would appear to be a reasonable, even a minimal, program which, if implemented, would more than pay for itself in contributing to improving the service program's efficiency and effectiveness, and to the rational allocation of scarce resources.

"Population research centers could foster interdisciplinary investigation of all aspects of population problems and attract our best scientific talents to apply their skills to what must certainly be considered a worthy challenge."

KENNETH J. RYAN, M.D.

Chairman, Department of Obstetrics & Gynecology
University of California School of Medicine, San Diego
La Jolla, California

Schering Award, 1950-1951
Ernest Oppenheimer Award, Endocrine Society, 1964

WE NEED POPULATION RESEARCH CENTERS

In the history of science, reproductive biology is still in its infancy. Although Aristotle authored the earliest books in embryology, the scientific world argued for two thousand years about whether babies were preformed and packaged as small people that grew or whether life and form developed from scratch. Leeuwenhoek saw sperm under the microscope and de Graaf described the ovary in the seventeenth century, but it was only in the 19th century that the egg was described and the endocrine function of the ovaries and testes was recognized. In the first third of this century, reproductive cycles and the hormones responsible for them were characterized. Since then the gains in knowledge of the code of life, molecular genetics, development and the control of reproduction have been spectacular. We have reached a point where expansion of existing fundamental knowledge, consolidation and application to man's needs can be realized.

Commitment of the scientific community not only to worry about, but

actively work in the area of population problems and reproductive biology has not been complete and needs rallying.

The National Academy of Sciences wrote a blueprint for population research in 1963 *(Growth of World Population),* but Federal support has still only been an unrealized promise. Political commitment has already been made in some recognition that there is or can be a population problem, but in the real world, commitment can be measured only in dollars and here only a halting start has been made.

Among our national priorities, we need one dedicated to the quality and quantity of human life. Population and reproductive research can fill this need.

For this purpose we need ten to fifteen population research centers in the United States with adequate support to provide the visibility, the avowed recognition and strength of purpose to stimulate interest and activity. Population research centers could foster interdisciplinary investigation of all aspects of population problems and attract our best scientific talents to apply their skills to what must certainly be considered a worthy challenge.

I estimate that a program of population research centers would require at least $15 million a year for a minimum period of 10 years.

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